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EVALUATION OF RATIONALITY IN PRESCRIBING FOR CARDIOVASCULAR DISORDERS IN INTENSIVE CARDIAC CARE UNIT: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT: Objective: To evaluate the prescribing pattern in patients admitted to intensive cardiac care unit, to evaluate direct cost of the treatment in patients admitted in intensive cardiac care unit, to evaluate the rationality of drugs prescribed and to prepare and submit therapeutic guideline for management of ACS. **Method:** This prospective observational study was carried out in ICCU for a period of ten months. Data were analysed for drug utilisation pattern and direct cost of treatment was calculated using patient's hospital and pharmacy bills. Rationality of therapy was evaluated based on class of recommendation from Indian guidelines for management of cardiovascular diseases, during the study period 70 prescriptions were screened. **Results:** The results show that a total of 156 (19.11%) cardiovascular drugs were prescribed to 70 patients admitted in ICCU during the study and anti-anginals 33 (21.15%) were equally used as inotropes 33 (21.15%), followed by anti-platelets 32 (20.51%), anticoagulants 27 (17%), hypolipidemics 21 (14%) and anti-arrhythmics 10(6%). Mean number of drugs per encounter was high (11), which contributed more to the cost of pharmacotherapy. 97.79% of the drugs belonged to NLEM, First class recommendation of Indian guidelines for management of cardiovascular diseases were followed in majority of prescriptions except for use of clopidogrel which belonged to class 2a recommendation for patients undergoing CABG surgery, this minor deviation was seen in 9 cases and the study has also noticed over use of antibiotics, it also revealed that ward bed charge, ICCU bed charge, ventilator charge had more contribution in direct medical cost of hospitalization. Cost of drug therapy accounted very less of direct medical cost of hospitalization. Cost of antimicrobials accounted 31.8% of cost of drug therapy. **Conclusion:** Irrational drug use in ICCU can be avoided by following standard treatment guidelines, This study will be helpful for hospital administration to monitor their hospital charges to affordable for patients and education to prescribers for affordable prescription of antimicrobials, improve rational drug use in ICCU and better management of patients.

INTRODUCTION: Cardiovascular diseases (CVDs) are showing an escalation among the Indian population with a trend of reaching the younger age groups.

It is now known to have a major share in the burden of diseases. A number of studies have been conducted time and again to find out the prevalence of CVDs and it has been found that they have a widespread prevalence in India, with regional variations. It is now affecting almost all sections of the society from young to old and most affluent to least affluent. Statistics also show an increased prevalence of CVDs in India compared to other developing countries. With the coming of the age of massive development, India has gone through

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dramatic lifestyle changes moving from agrarian diets and active lifestyles to fast foods and sedentary lifestyles in a much shorter span of time than other nations. Consequently, mortality rates related to chronic non-communicable diseases like cardiovascular diseases (CVDs), coronary heart diseases (CHDs), diabetes and stroke have increased rapidly in the last decade with CVDs having a major share¹.

Cardiovascular diseases (CVDs) account for >17 million deaths globally each year (30% of all deaths), 80% of which occur in low-income and middle-income countries, and this figure is expected to grow to 23.6 million by 2030. Ischaemic heart disease alone caused 7 million deaths worldwide in 2010, an increase of 35% since 1990. Commencing in 1980, the Global Burden of Disease Study has provided the most-comprehensive estimates of disease burden for 235 causes of death and the disease burden attributable to 67 different risk factors in 21 regions of the world. Non-communicable diseases, of which CVDs are the most prevalent, cause the greatest morbidity and mortality worldwide. Eliminating obesity, unhealthy diets, and physical inactivity could prevent up to 80% of heart disease, stroke, and diabetes mellitus².

Coronary heart disease (CHD) is the largest contributor to CVD; its incidence and the prevalence of important risk factors varies greatly according to geographical region, sex, and ethnic background. According to recent study by registrar of India (RGI) and the Indian council of medical research (ICMR), about 25 percent of deaths in the age group of 25-69 years occur because of heart diseases. If all age groups are included, heart diseases account for about 19 percent of all deaths. It is the leading cause of death among males as well as females and in all regions in India, the study found. Half of all heart attacks in this population occur under the age of 50 years and 25 percent under the age of 40³.

Acute coronary syndromes (ACS) and acute myocardial infarction, acute decompensated heart failure (HF), arrhythmias, and various other cardiac conditions are emergencies that require specialized equipped intensive cardiac care unit (ICCU) setup to perform life saving emergency interventions like

fibrinolysis, primary percutaneous coronary intervention (PCI), and defibrillation. Certain drugs like antiplatelet, anticoagulants, and fibrinolytics are needed to be administered at the earliest to these critical patients¹¹. There are many drugs prescribed in a single patient simultaneously in ICCU with the aim of maximizing efficacy in a particular condition¹². Prescribing rationally in ICCU is important to minimize chances of drug interactions, adverse drug reactions, and unduly high cost of treatment. Rationality of drug prescriptions can be analyzed based on class of recommendation from Indian guidelines for management of cardiovascular diseases⁵, this study was aimed to evaluate prescribing pattern and direct cost of therapy in patients admitted in ICCU.

Aim of the Study:

- To evaluate the prescribing pattern in patients admitted to intensive cardiac care unit.
- To evaluate direct cost of the treatment in patients admitted to intensive cardiac care unit.
- To evaluate the rationality of drugs prescribed.
- To prepare and submit therapeutic guideline for management of ACS.

METHODS: This was a prospective observational study performed in ICCU for a period of 10 months. The inclusion and exclusion criteria's were:

Inclusion Criteria:

- All Patients of all age, of either sex admitted in intensive cardiac care unit (ICCU) with cardiovascular diseases.

Exclusion Criteria:

- Patients with insufficient data and those who are not willing to participate in the study.

Methodology: A prospective observational study was carried out in ICCU of a tertiary teaching care hospital after obtaining approval from hospital ethics committee. All the patients of all age, of either sex admitted in the ICCU during the study

period were enrolled in the study. Patient demographic data like name, age, sex, address, socioeconomic class were recorded on the specially designed case record form. Patient's clinical data including diagnosis, detailed history of illness, past history, family history was noted. The details of drug therapy including the drug prescribed, dose, frequency, and duration of the treatment was noted in the case record form.

Government of India reported that the private sector delivers about 60% of all inpatient care. In India, during hospitalization 80% patients have to pay out of their pocket for health care service due to lack of insurance cover and more than 40% admitted patient had to borrow money or sell their assets¹³. Information about cost of hospitalization is helpful for policy makers to allocate better health facilities and services. It is also helpful in developing country for reimbursement of social security system¹⁰.

There is lack of data about direct medical cost of hospitalization in admitted patients at private hospital in southern India. Hence this study was carried out to analyze direct medical cost of hospitalization and cost of drug therapy in admitted patients at private hospital in Coimbatore City of southern India. Direct cost of treatment was calculated using patient's hospital and pharmacy bills. The cost of drugs was obtained from commercial publications like Indian Drug Review 2015 and current index of medical specialties (CIMS) online. Direct medical cost, was analyzed. Cost of hospital bed charge, laboratory charge, diagnostic charge, doctor consulting charge, etc. were included in direct medical cost.

Prescribed drugs were analyzed for inclusion in National List of Essential Medicines (NLEM)³, India, 2015 and Essential Drug List (EDL) of World Health Organization (WHO)⁴, 2015. Rationality of therapy was evaluated based on class of recommendation by referring to Indian guidelines for management of cardiovascular diseases⁵.

To know direct medical cost, collected data of 70 admitted patients' billing record were analysed. Data was selected from patient's i.p. registration number. Data like age, gender, admission in ICCU,

outcome of patient, cost of hospitalization including investigation charges, doctor consulting charge, ICCU charge etc. were recorded in preformed case record form. Direct medical cost, total cost of drug therapy and cost of group of drugs were calculated.

RESULTS: A total of 70 patients were enrolled in the study over duration of 10 months. Mean age of patients was 35.92 years. Out Of the 70 patients who have undergone treatment in ICCU, 39 (56%) were male and remaining was female. Majority of the patients belonged to age group of 40-60 years, which comprised around 32.8% of the total patients, mean stay in ICCU was 2.14 days (range 1-5), most of the patients presented with chest pain and breathlessness.

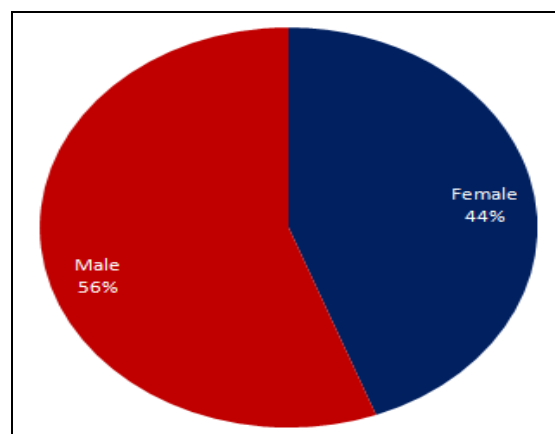


FIG. 1: GENDER DISTRIBUTION

Majority of the patients admitted in ICCU were diagnosed to have Ischemic heart diseases 23 (32.85%) patients, followed by a trial septal defect (ASD), 16 (23.14%) patients and Rheumatic heart diseases (RHD), (18.57%) patients. Diabetes mellitus in 7 (10%) and Hypertension in 5 (7.14%) patients were the frequently associated co-morbid conditions.

A total of 156 (19.11%) cardiovascular drugs were prescribed and anti-anginals 33 (21.15%) were equally used as inotropes 33 (21.15%), followed by antiplatelets 32 (20.51%), anticoagulants 27 (17%), hypolipidemics 21 (14%) and anti-arrhythmics 10 (6%). Out of the total 70 patients, among anti-anginal drugs prescribed to patients, nitroglycerine 11 (7%) was widely used followed by, isosorbide dinitrate 5 (3.2%), Trimetazidine 5 (3.2%) and Ivabradine 3 (1.92%).

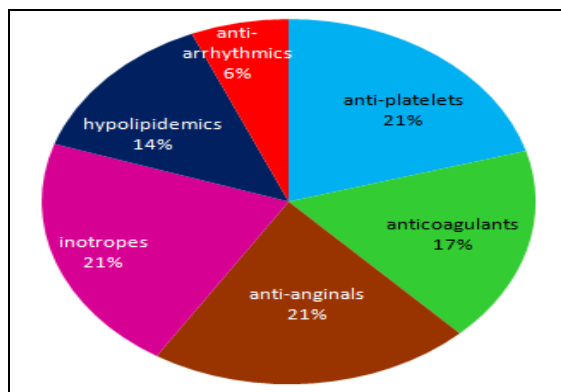


FIG. 2: CARDIOVASCULAR DRUGS

Digoxin 18 (11.53%) was the frequently prescribed inotropes, followed by dobutamine 7 (4.48%), Aspirin and clopidogrel alone or the combination of aspirin and clopidogrel were the commonly used antiplatelet drugs. Out of the total 32 patients who received antiplatelet therapy 13 were given dual antiplatelet drug combination.

Among anticoagulants, Acenocoumarol was widely used 19 (12.17%) followed by Heparin 7 (4.48%), only 11 antiarrhythmics were prescribed, amiodarone 5 (3.2%), isoprenaline 5 (3.2%) and lignocaine 1 (0.64%). Opioid analgesics were used and morphine was used in 37 (52%) patients followed by fentanyl 29 (41.42%) patients. Antihypertensives were among the most prescribed drugs accounting 15% (125) of all the drugs, Diuretics are the most prescribed group 90 (72%) and furosemide is the most widely used anti hypertensive drug 67 (53%) followed by metoprolol 14 (11.2%) and spironolactone 11 (8.8%).

Apart from cardiovascular drugs, use of drugs that reduce gastric secretion, mainly Ranitidine was seen in 49 (70%) cases as prophylaxis against gastritis and ondansetron was the most widely used

antiemetics. Antibiotics were prescribed in all the cases with total of 78 antibiotics, among them 66 (84.61%) were cephalosporins and ceftriaxone was used in 54 (77.14%) cases as prophylaxis followed by cefotaxime 9 (12.85%) cases.

Type of the Surgery Performed: Total of 80 surgeries were done on 70 patients in ICCU during the study, CABG was used in 27 (33.75%) cases being the most widely used technique, followed by ASD closure 17 (21.25%) and Mitral valve replacement 16 (20%).

TABLE 1: TYPES OF SURGERIES PERFORMED

| S. no | Types of Surgery | No of cases | Percentage % |
|-------|--------------------------------|-------------|--------------|
| 1 | ASD closure | 17 | 21.25 |
| 2 | Bi-directional glenn operation | 1 | 1.25 |
| 3 | BT shunt ligation | 1 | 1.25 |
| 4 | CABG | 27 | 33.75 |
| 5 | ICR (intra-cardiac repair) | 6 | 7.5 |
| 6 | LA clot removal | 3 | 3.75 |
| 7 | Mitral valve replacement | 16 | 20 |
| 8 | Resectioning muscle bundle | 1 | 1.25 |
| 9 | tricuspid valve repair | 1 | 1.25 |
| 10 | VSD closure | 7 | 8.75 |

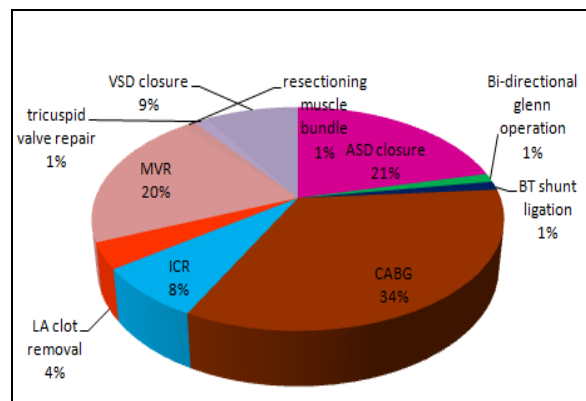


FIG. 3: SURGERIES PERFORMED

TABLE 2: DETAILS OF DRUG THERAPY DURING HOSPITALIZATION IN ICCU

| S. no | Details of drug therapy during hospitalization | Number |
|-------|--|--------|
| 1 | Total number of prescriptions analyzed | 70 |
| 2 | Total number of drugs prescribed | 816 |
| 3 | Average number of drugs per patient | 11.65 |
| 4 | Number of injections out of total number of drugs prescribed | 490 |
| 5 | Average number of injections per patient | 7 |
| 6 | Total number of drugs administered orally | 343 |
| 7 | Average number of oral drugs per patient | 4.97 |
| 8 | Total number of inhalers | 19 |
| 9 | Total number of Cardiovascular drugs out of total number of drugs prescribed | 156 |
| 10 | Cardiovascular drugs from the essential drug list | 152 |
| 11 | Cardiovascular drugs out of essential drug list | 4 |
| 12 | Total number of drugs from essential drug list | 798 |

Direct Cost of Treatment in ICCU: Mean cost of drug treatment per patient was 1897.56, Mean total cost of hospitalization incurred per patient was Rs 1,02,024.69. Around 60% of all drugs prescribed were administered parenterally and they were responsible for 76.06% cost burden of total cost of pharmacotherapy followed by oral drugs which took 19.94% of total cost of pharmacotherapy.

Analysis of Drugs Inclusion in NLEM and EDL of WHO: Prescribed drugs were analyzed for inclusion in national list of essential medicines (NLEM), India, 2015³ and essential drug list (EDL) of world health organization (WHO)⁴, the study revealed that out of 816 drugs prescribed 798 (97.79%) were included in NLEM and 783 (95.95%) were also included in EDL of WHO. Evaluation of rationality in prescribing was done by comparing prescription pattern of all 70 cases to class of recommendation given by Indian guidelines for management of cardiovascular diseases⁵. Apart from use of clopidogrel which belonged to class 2a for patients undergoing CABG in 9 patients, all the other prescribed drugs were according to class 1 recommendation of Indian guidelines for management of cardiovascular diseases, the study has noticed over usage of antibiotics, more than 3 days in 60% of cases, which is irrational according to CDC guidelines⁶.

DISCUSSION: This study was carried out with the aim to analyse prescribing pattern, the rationality of treatment, and to estimate direct treatment cost in ICCU. Mean age of patients in our study was lower compare to Indian study by Patel *et al.*,⁷ The possible explanation to this fact could be the presence of congenital heart diseases which were more prevalent in young patients. The majority of the patients in our study were males which is similar to earlier Indian and foreign studies. In our study, prevalence of hypertension and type-2 diabetes is generally low compare to that of an Indian study performed in a cardiac unit. The pattern of comorbid conditions may vary with the study population.

Mean stay in ICCU was lower 2.14 as compared with an Indian study in ICCU that reported 3.07 ± 1.39 days. The possible reason may be due to difference in practicing policies in different hospital ICCUs. Most common diagnosis was IHD,

which is comparable with earlier Indian study and a study from Malaysia^{8,9}. In Indian studies, mean number of drugs was more than 11, which was also seen in our study, in contrast to a foreign study that reported less than 10 drugs. This can be due to difference in morbidity pattern and the different prescribing practices in different countries. As per Indian guidelines for management of cardiovascular diseases, there are three classes of recommendations. Class 1 drugs are those having highest benefit risk ratio and recommended.

Class 2 drugs are those with somewhat less benefit risk ratio compared with class 1 and are probably recommended. Class 3 drugs are those that are not recommended or potentially harmful. In our study, considering the rationality based on Indian guidelines for management of cardiovascular diseases for ACS, as far as drug therapy is concerned, majority of prescriptions adhered to the guidelines in form of class 1 and class 2 recommendations. None of the drugs belonging to class 3 were prescribed. Use of inotropes, beta-blockers, and vasodilators in HF patients was according to standard Indian guidelines for management of cardiovascular diseases for acute HF. The proton pump inhibitors (PPI) could lead to therapeutic ineffectiveness of clopidogrel because this metabolic enzyme-CYP2C19-is responsible for its bioactivation. So, wide use of PPIs needs a "watchful eye" when co-prescribed with other drugs.

Most commonly prescribed antimicrobial drug group was third generation cephalosporin in our study, which was similar to an Indian study. Cardiac interventions are clean surgeries according to Centers for Disease Control and Prevention CDC guidelines⁶, ceftriaxone, which is a third generation cephalosporin having excellent Gram-positive coverage should be used for prophylaxis against the development of surgical site infection. Prescribers in our setup used antibiotics for more than 3 days, which is irrational according to CDC guidelines. Use of antibiotics for extra days will contribute more to the cost of pharmacotherapy.

Mean cost of pharmacotherapy was higher than that of an Indian study (1897.56Rs). Among all the drugs, 60% were administered parenterally adding

to a significant cost burden to the patient. About 76.03% of total cost of pharmacotherapy was attributed to these parenteral drugs. This finding was comparable with an Indian study. Our study had a few limitations, there was no follow up after discharge from the ICCU. We did not estimate the indirect cost, which includes daily wages loss, transportation cost, and so forth. Focusing on drug therapy in ICCU would be helpful to cardiologists in improving prescribing policies. Future studies can focus on drug use in ICCU and outcomes like adverse, drug, reactions and actual, drug-drug, interactions.

CONCLUSION: In conclusion, our study revealed that anti-anginal drugs and inotropics were the most frequently prescribed cardiovascular drug groups in ICCU. Mean number of drugs per encounter was high, which contributed more to the cost of pharmacotherapy. Most of the drugs belonged to NLEM. First class recommendation of Indian guidelines for management of cardiovascular diseases were followed in majority of prescriptions except for use of clopidogrel which belonged to class 2a and overuse of antibiotics was found to be a major deviation according to CDC guideline.

Our study also revealed that ward bed charge, ICCU bed charge, ventilator charge had more contribution in direct medical cost of hospitalization. Cost of drug therapy accounted very less of direct medical cost of hospitalization. Cost of antimicrobials accounted 31.8% of cost of drug therapy. This study will be helpful for hospital administration to monitor their hospital charges to affordable for patients and education to prescribers for affordable prescription of antimicrobials, improve rational drug use in ICCU and better management of patients.

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CONFLICT OF INTEREST: Authors do not have any conflict of interest.

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